



EXHIBIT 1



Application No. 09/646,807
Amendment dated December 28, 2006
Reply to Office Action of June 28, 2006

Docket No. 025122.0101P3US
(Previously 023004.0104P3US)

AMENDMENTS TO THE CLAIMS

1. - 55. (Canceled)

56. (Currently Amended) A ~~synthetic~~-isolated genetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in a ~~mammal-eukaryotic~~ cell which is transfected with said genetic construct, said genetic construct comprising ~~at least two~~ copies of a ~~target structural~~ gene sequence ~~or region thereof~~, wherein said ~~at least two~~ copies are ~~at least 80% having greater than 20 consecutive nucleotides which is identical in sequence to greater than 20 consecutive nucleotides of said target gene or region thereof~~, and wherein said at least two copies are placed operably under the control of a single promoter sequence and a transcription termination sequence each of which is operable in said cell, wherein ~~at least one~~ copy is placed operably in the sense orientation under the control of said promoter sequence and ~~wherein at least one other copy is placed operably in the antisense orientation under the control of said promoter sequence~~, and wherein said two copies are spatially separated by a stuffer fragment which comprises a sequence of nucleotides.

57. (Currently Amended) An ~~isolated~~-~~synthetic~~ genetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in a ~~mammal-plant~~ cell which is transfected with said genetic construct, wherein said genetic construct comprises ~~at least two~~ copies of a ~~target structural~~ gene sequence having greater than 20 consecutive nucleotides which is identical in sequence to greater than 20 consecutive nucleotides of said target gene, or region thereof ~~and wherein~~ each copy is separately placed under the control of a promoter and a transcription termination sequence each of which is operable in said cell, ~~and wherein said copies are at least 80% identical to said target gene or a region thereof~~, wherein at least one copy is placed operably in the sense orientation under the control of an individual promoter sequence, and wherein at least one other copy is placed operably in the antisense orientation under the control of another individual promoter sequence, and wherein said two copies are spatially separated by a stuffer fragment which comprises a sequence of nucleotides.

58. (Cancelled)

59. (Currently Amended) The ~~isolated synthetic~~ genetic construct ~~according to any one of~~ claims 56-~~57~~8 wherein the target gene encodes a viral DRNA polymerase, viral RNA polymerase or viral coat protein and said region of the target structural gene sequence is 20 to 30 nucleotides long.
60. (Currently Amended) The isolated genetic construct ~~according to any one of claims 56-~~ ~~57~~8 wherein said region of the target structural gene sequence is ~~at least~~ 30 nucleotides long.
61. (Cancelled).
62. (Currently Amended) An eukaryotic cell comprising the genetic construct ~~according to of~~ claim 56, wherein the synthetic genetic construct is transcribed in the cell9.
63. (Currently Amended) A ~~mammal-plant~~ cell comprising the genetic construct ~~according to of~~ claim 57, wherein the synthetic genetic construct is transcribed in the cell60.
64. (Cancelled).
65. (New) The genetic construct of claim 56, which is in a virus particle which is an attenuated virus or associated with a virus coat.
66. (New) The genetic construct of claim 56, which is encapsulated in a liposome.
67. (New) The genetic construct of claim 56, which is integrated into the genome of the cell.
68. (New) The cell of claim 62, wherein the target gene is a viral genetic sequence.
69. (New) The cell of claim 62, wherein the target gene is a nucleotide sequence of a viral pathogen of an animal cell.
70. (New) The cell of claim 62, wherein the target gene is from a retrovirus.
71. (New) The cell of claim 62, wherein the target gene is from an immuno deficiency virus.

72. (New) The cell of claim 62, wherein the target gene is from a single-stranded (+) RNA virus.
73. (New) The cell of claim 62, wherein the target gene is from a double-stranded DNA virus.
74. (New) The cell of claim 62, wherein the target gene is a transgene in the cell.
75. (New) The cell of claim 62, wherein the target gene is a member of a multigene family in the cell.
76. (New) The cell of claim 62, wherein the target gene is an endogenous gene of the cell.
77. (New) The cell of claim 62, wherein the greater than 20 consecutive nucleotides of the target gene corresponds to a coding region of the target gene.
78. (New) The cell of claim 62, wherein the greater than 20 consecutive nucleotides of the target gene corresponds to a 5'- or 3'- untranslated sequence of the target gene.
79. (New) The cell of claim 62, wherein a transcribed region of the genetic construct comprises an intron.
80. (New) The cell of claim 62, wherein the stuffer fragment is a sequence of nucleotides 10-50 nucleotides in length, 50-100 nucleotides in length, or 100-500 nucleotides in length.
81. (New) The cell of claim 62, wherein the stuffer fragment comprises an intron.
82. (New) The cell of claim 62, wherein the total length of said structural gene sequences is no more than 2.0 kilobases.
83. (New) The cell of claim 82, wherein the total length of said structural gene sequences is no more than 0.5 kilobases.

84. (New) The cell of claim 62, wherein the two copies are in a head-to-head orientation relative to each other.
85. (New) The cell of claim 62, wherein the two copies are in a tail-to-tail orientation relative to each other.
86. (New) The cell of claim 62, wherein the promoter is heterologous with respect to the structural gene sequence.
87. (New) The cell of claim 62, wherein the promoter is expressed before the commencement of detectable expression of the target gene in the cell.
88. (New) The cell of claim 62, wherein the genetic construct is expressed to produce a primary transcript which has a polyadenylate sequence added to the 3'-end.
89. (New) The cell of claim 62, which is an animal cell.
90. (New) The cell of claim 89, wherein the animal is a vertebrate animal.
91. (New) The cell of claim 89, wherein the animal is an invertebrate animal.
92. (New) The cell of claim 89, wherein the animal is an aquatic animal.
93. (New) The cell of claim 89, wherein the animal is an insect.
94. (New) The cell of claim 89, wherein the animal is a fish.
95. (New) The cell of claim 89, wherein the animal is a bird.
96. (New) The cell of claim 89, wherein the animal is a mammal.

- 97. (New) The cell of claim 62, wherein the cell is a human cell in cell culture.
- 98. (New) The cell of claim 89, wherein the cell is a somatic cell.
- 99. (New) The cell of claim 89, wherein the cell is a haematopoietic stem cell.
- 100. (New) The cell of claim 89, wherein the cell is a T-cell.
- 101. (New) The cell of claim 62, wherein the cell is in tissue culture.
- 102. (New) The cell of claim 62, which is a multicellular plant cell.
- 103. (New) The cell of claim 102, which is a monocotyledonous plant cell or a dicotyledonous plant cell.
- 104. (New) The cell of claim 102, which is in a transgenic plant.
- 105. (New) The cell of claim 104, wherein the transgenic plant has a reduced level of expression of the target gene.
- 106. (New) The cell of claim 104, wherein the transgenic plant exhibits virus resistance.
- 107. (New) An isolated eukaryotic cell, tissue or organ, comprising the genetic construct of claim 56.